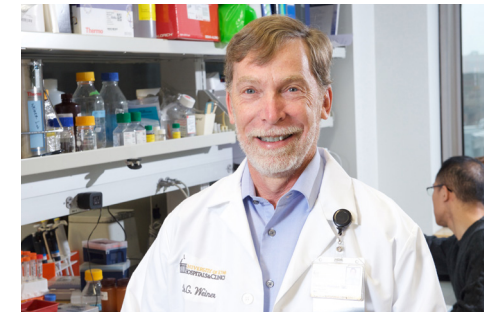


UNIVERSITY OF IOWA
**HOLDEN COMPREHENSIVE
CANCER CENTER**
2019 ANNUAL REPORT



THE MISSION OF HOLDEN COMPREHENSIVE CANCER CENTER IS TO
**DECREASE THE PAIN AND SUFFERING CAUSED BY CANCER
IN IOWA, SURROUNDING COMMUNITIES, AND THE WORLD.**
WE DO THIS THROUGH IMPROVED CANCER PREVENTION AND
TREATMENT BASED ON THREE INTERDEPENDENT MISSIONS OF
RESEARCH, CLINICAL SERVICE, AND EDUCATION.

MESSAGE FROM THE DIRECTOR → [WATCH ADDRESS](#)



In research, education, and clinical care, 2019 was an incredibly exciting year at University of Iowa Holden Comprehensive Cancer Center. The speed of progress has never been greater. This progress includes making basic science discoveries about the very nature of cancer and the behavior of cancer in the body, and applying these advances to the care we provide for our patients every day. National and local data speak to a decreasing burden of cancer, yet we should not be satisfied—we know we still have a long way to go.

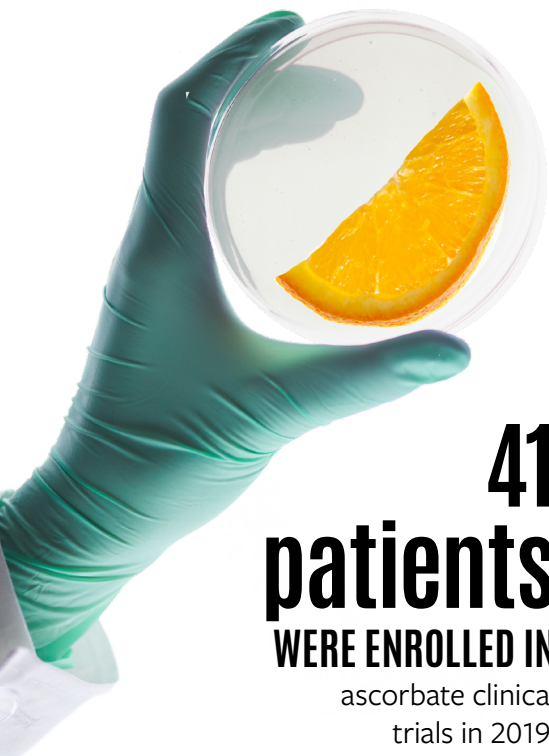
At Holden, we conduct the full spectrum of basic, clinical, and population research, we educate the next generation of cancer caregivers and cancer researchers, and we provide world-class interdisciplinary cancer care. Doing any one of these things well requires that we do all three of them well. When our students generate new ideas, they help us conduct better research, and that research benefits our patients.

One of the unique aspects of Holden is the structure of our multidisciplinary oncology groups, or MOGs. We have 12 MOGs, each focused on a specific cancer type. Within these MOGs, researchers and clinicians work together to take the advances made in the lab and bring them to patients as quickly and efficiently as possible. This includes enhancing our ability to apply what we already know about cancer prevention, development of new cancer screening tools, expanding the number of patients who benefit from advances such as cancer immunotherapy, and working to develop new approaches to enhancing the quality of life for cancer survivors.

Another unique aspect of our program is the way we expose PhD students in our cancer biology program to clinical care. Each student spends time with our clinical oncologists, observing patients as they receive their care. Our students often speak of the value of that experience. It helps them think about cancer as more than a subject of study and helps them recognize that advances they make in the research laboratory can have a major and positive impact on the everyday lives of the people we serve.

While I am enthusiastic about what we achieved in 2019, the future looks even better. The speed of progress continues to accelerate, which means 2020 is sure to be an even more exciting year in our effort to reduce the burden of cancer for the people of Iowa and beyond.

George J. Weiner, M.D.
Director
University of Iowa Holden Comprehensive Cancer Center



41
patients
WERE ENROLLED IN
ascorbate clinical
trials in 2019.

TAKING ANOTHER LOOK AT VITAMIN C

Holden researching high-dose vitamin C with multiple clinical trials

Using a five-year, \$9.7 million grant from the National Cancer Institute in 2017, researchers at Holden Comprehensive Cancer Center are testing high-dose, intravenous (IV) vitamin C in the treatment of three of the deadliest cancers affecting the U.S. population: pancreatic cancer, non-small cell lung cancer, and glioblastoma multiforme.

The major clinical trials funding is vindication of decades of basic and translational research that pushed back against deep skepticism of vitamin C's utility as a cancer therapy. These earlier studies showed that at millimolar concentrations, achievable only through IV administration, vitamin C acts as a prooxidant and makes cancer cells more susceptible to the effects of chemotherapy and radiation.

“Success in this project would suggest that adding high-dose IV vitamin C to cancer treatment protocols could be a safe, simple, and cost-effective approach to

improving treatment for many kinds of cancer,” says Joseph Cullen, MD, University of Iowa professor of surgery and co-PI on the grant along with Douglas Spitz, PhD, UI professor of radiation oncology. “If the results from our early- and mid-phase clinical trials are positive, the next step would be to test this therapy in large, stage 3 clinical trials that could lead to approval of this approach and have a powerful and lasting impact on clinical cancer care in the coming years.”

Continued integration of the clinical work with basic research will also allow the team to determine whether certain biomarkers or functional imaging tests can be used to predict which cancers might be most susceptible to treatment with high-dose vitamin C.

More trials using high-dose vitamin C to treat plasma cell disorders and sarcoma were launched at Holden in 2019.



Focusing on immunotherapy lymphoma research, doctoral student Shakoora Sabree pipettes microcentrifuge tubes.

IMPROVING THE STANDARD OF CARE FOR METASTATIC MELANOMA

Holden investigators are at the forefront of basic research into a class of molecules that stimulate the immune system known as TLR9 agonists. Holden researchers discovered the role of TLR9 agonists and demonstrated their anti-cancer effects.

Now a Holden-led phase 1b clinical trial that combines a TLR9 agonist with pembrolizumab (Keytruda) has shown durable responses in patients with PD-1 resistant metastatic melanoma.

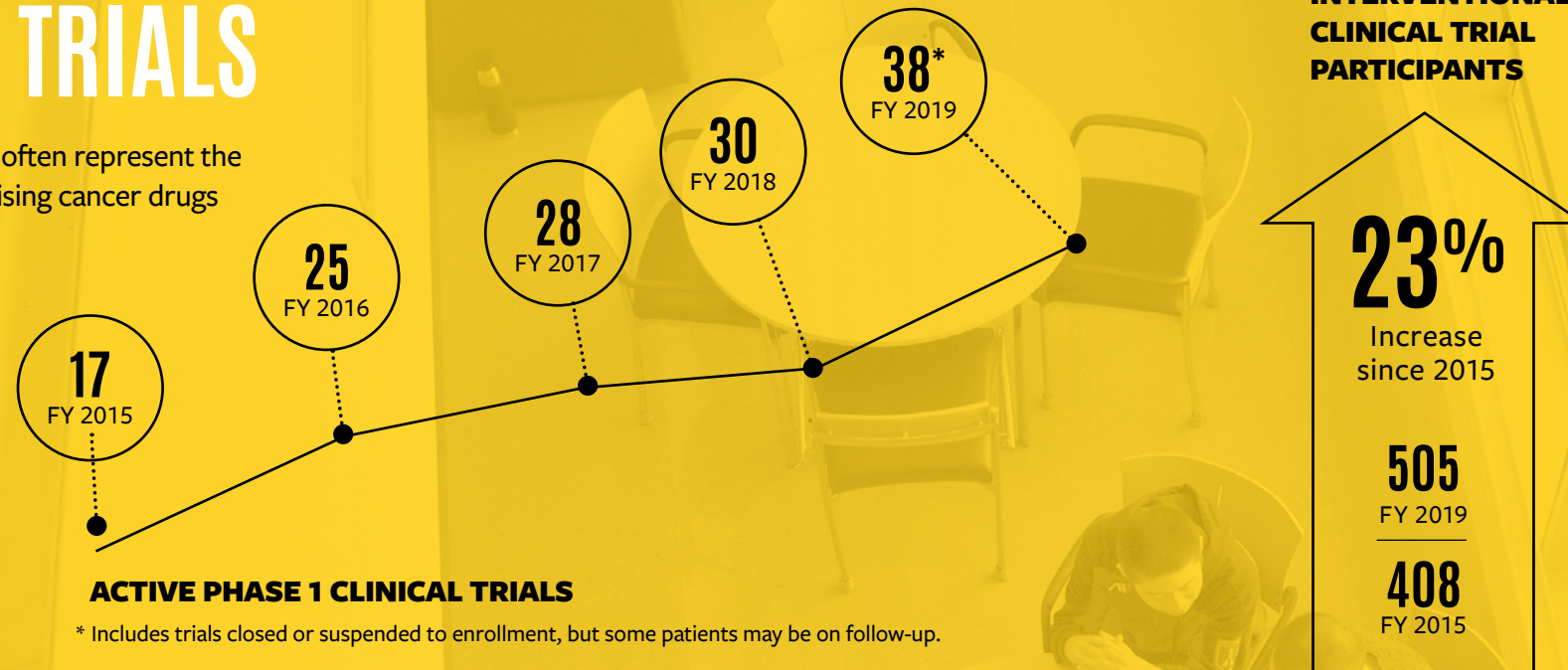
Results from the ongoing study were presented at the 34th annual meeting of the Society for Immunotherapy of Cancer in November 2019.

University of Iowa oncologist Mohammed Milhem, MBBS, principal investigator, says the trial addresses the fact that more than 50 percent of patients develop resistance when treated with pembrolizumab alone.

“Finding safe and effective therapies for these patients is critical,” Milhem says.

CLINICAL TRIALS

Early phase clinical trials often represent the first human use of promising cancer drugs and therapies.



RESEARCH FUNDING

2019 HOLDEN PROGRAMS



\$34 MILLION+
Total funding for the last 5 years

PARTNERS IN COLLABORATION

Holden researchers, clinicians, and members collaborate with a number of other organizations through partnerships in the Big Ten Cancer Research Consortium, ORIEN, and the Alliance for Clinical Trials in Oncology, among others. These collaborations allow partnering institutions to combine resources and expertise to launch innovations in research and develop new approaches to treatment.



PUBLISHED PAPERS

This is a small sample of notable manuscripts recently published by University of Iowa researchers.

Umesalma S, Kaemmer CA, Kohlmeier JL, Letney B, Schab AM, Reilly JA, Sheehy RM, Hagen J, Tiwari N, **Zhan F**, Leidinger MR, **O'Dorisio TM**, **Dillon J**, Merrill RA, Meyerholz DK, Perl AL, Brown BJ, **Braun TA**, Scott AT, Ginader T, Taghiyev AF, **Zamba GK**, **Howe JR**, Strack S, **Bellizzi AM**, Narla G, **Darbro BW**, Quelle FW, **Quelle DE**. RABL6A inhibits tumor-suppressive PP2A/AKT signaling to drive pancreatic neuroendocrine tumor growth. *J Clin Invest*. 2019; 130:1641-53.

Loriot Y, Necchi A, Park SH, Garcia-Donas J, Huddart R, Burgess E, Fleming M, Rezazadeh A, Mellado B, Varlamov S, Joshi M, Duran I, Tagawa ST, **Zakharia Y**, Zhong B, Stuyckens K, Santiago-Walker A, De Porre P, O'Hagan A, Avadhani A, Siefker-Radtke AO. Erdafitinib in locally advanced or metastatic urothelial carcinoma. *NEJM*. 2019; 381(4):338-348.

Anderson CM, Lee CM, Saunders DP, Curtis A, Dunlap N, Nangia C, Lee AS, Gordon SM, Kovoor P, Arevalo-Araujo R, Bar-Ad V, Peddada A, Colvett K, Miller D, Jain AK, Wheeler J, Blakaj D, Bonomi M, Agarwala SS, Garg M, Worden F, Holmlund J, Brill JM, Downs M, Sonis ST, Katz S, **Buatti JM**. Phase IIb, randomized, double-blind trial of GC4419 versus placebo to reduce severe oral mucositis due to concurrent radiotherapy and cisplatin for head and neck cancer. *J Clin Oncol*. 2019; 37(34):3256-3265.

Wang Y, **Farooq U**, **Link BK**, Larson MC, King RL, Maurer MJ, Allmer C, Hefazi M, Thompson CA, Micallef IN, Johnston PB, Habermann TM, Witzig TE, Ansell SM, Cerhan JR, Nowakowski GS. Late relapses in patients with diffuse large B-cell lymphoma treated with immunochemotherapy. *J Clin Oncol*. 2019; 37(21):1819-27.

CLINICAL CONNECTION GIVES STUDENTS **NEW INSIGHT**

A unique clinical connections component in the University of Iowa's cancer biology graduate program has given doctoral candidate Keith Garcia new insight into his research.

Garcia, a doctoral student in the laboratory of Munir Tanas, MD, is among a number of graduate students enrolled in the semester-long course, which provides the opportunity to shadow clinical oncologists in settings such as genetic counseling, pathology, radiation oncology, and surgery.

"The shadowing was pretty eye-opening," says Garcia, who chose the UI after completing his undergraduate degree in microbiology at the University of Texas at Austin and coursework at Texas State University.

The goal of the course is to help students identify clinically relevant

questions that can lead to novel cancer research projects.

Garcia shadowed sarcoma specialist Varun Monga, MD, clinical assistant professor of internal medicine in hematology, oncology, and blood and marrow transplantation, and Mohammed Milhem, MD, Holden Chair of Experimental Therapeutics and associate director of clinical research at Holden Comprehensive Cancer Center.

"I specifically chose sarcoma because that's what my research is based on," says Garcia, whose dissertation focuses on understanding the role of the Ada2a-containing histone

acetyltransferase complex in mediating activity of the TAZ-CAMTA1 and YAP-TFE3 fusion proteins.

He also participated in and learned from tumor boards and shadowed oncologists as they met with patients.

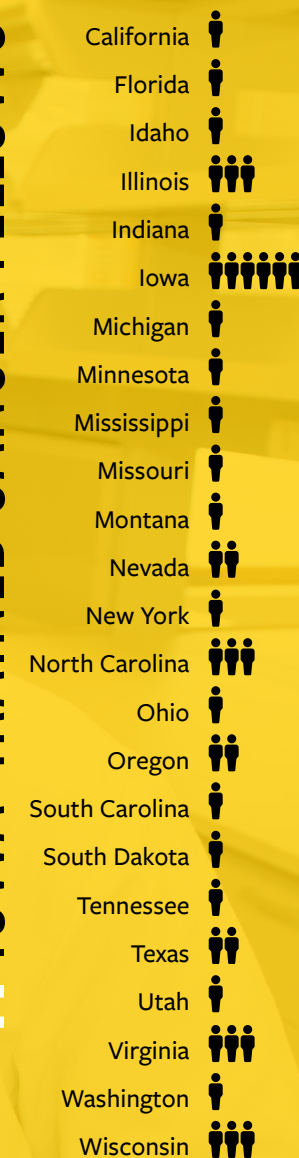
"I witnessed pretty much everything," Garcia says, adding that the experience gave him a heightened sense of urgency. "Seeing these patients pushes me to discover biology that could possibly be targeted in the clinic."

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Doctoral student Keith Garcia and Munir Tanas, MD, collaborate on sarcoma research at the Holden Cancer Research Laboratories.

TRAINING THAT SPANS THE NATION

41 IOWA-TRAINED CANCER FELLOWS

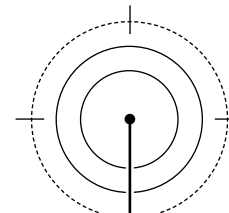


Physician practice locations of 2014-2019 graduates of gynecologic oncology, head and neck cancer, medical hematology oncology, and dermatology fellowships.

CANCER BIOLOGY

PHD CANCER PROGRAM APPLICANTS





1 of first 3 U.S. CANCER CENTERS

to start treating cancers with MR-linac technology that combines a 1.5 Tesla MRI scanner and a linear accelerator

TARGETING TUMORS WITH PINPOINT ACCURACY

Holden is early adopter of technology blending high-quality imaging with radiation therapy

A new radiation therapy device, MR-linac, simultaneously combines state-of-the-art imaging with radiation treatment for unprecedented accuracy in attacking tumors.

In May Holden became one of the first three U.S. cancer centers to treat patients with the 1.5 Tesla Elekta Unity MR-Linac. MR-linac features a high field-strength MRI scanner, making it the world's first radiation therapy technology to combine a high field-strength MRI scanner with a linear accelerator in one system.

Doctors using MR-linac can "see" tumor tissue more clearly and customize the radiation dose during treatment. Because it can safely deliver higher doses of radiation to a tumor, MR-linac can greatly improve outcomes for patients

with tumors in the prostate, brain, pancreas, liver, and lung.

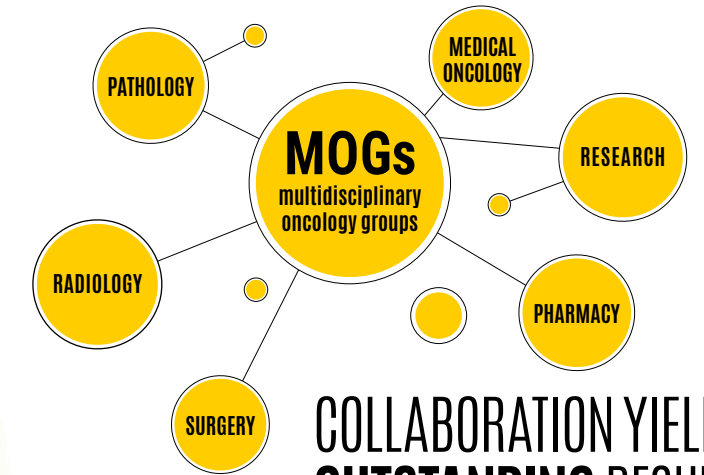
"The ability to view tissue with MR-linac versus CT is remarkable," says John Buatti, MD, chair of the University of Iowa Department of Radiation Oncology and a Holden member. "The high-Tesla magnet combined with linac provides significantly better images than previous technology."

Buatti leads the team using MR-linac to personalize cancer treatment. He predicts the machine will be the busiest MR-linac in the country, eventually treating approximately 175 patients annually as the therapy becomes more widely known.

Buatti also expects the University of Iowa to become an MR-linac training center.



Travis White and his wife Judy visit University of Iowa Holden Comprehensive Cancer Center, where he received multidisciplinary care.



COLLABORATION YIELDS OUTSTANDING RESULTS

Sarcoma trial accrual demonstrates value of true collaboration in Holden MOGs

Just weeks after Holden began recruiting patients for a collaborative phase II sarcoma trial, the trial's organizers reached out with a question.

"They said, 'You're putting a lot of patients into this trial. How are you doing it?'" says Holden oncologist Mohammed M. Milhem, MBBS. "What they meant was, 'How do you get opinionated, highly educated leaders in their fields to agree so consistently?'"

The answer, Milhem says, is in the collaborative, patient-focused culture that defines every multidisciplinary oncology group (MOG) at Holden.

"Our ability to make group decisions was built on a philosophy created long before we'd evaluated a single patient," Milhem says. "Everyone on the board bought into a collaborative approach when they joined. We all agreed that we'd focus on the trial as an important resource for patients."

The result: quick consensus. And Holden remains the trial's accrual leader.

THE NATION'S LEADER IN NEUROENDOCRINE TUMOR RESEARCH AND PATIENT CARE

With FDA approval in 2019 of a new drug to identify somatostatin receptor positive neuroendocrine tumors, Holden added to its reputation as an unparalleled NET research center.

HOLDEN CLINICAL CARE

A YEAR OF GROWTH

10 

New providers

15 

New clinical exam rooms

CARING FOR THE COUNTRY



PATIENTS FROM **47 STATES**

including Alaska and Hawaii—FY 2019

PATIENT CARE TRENDS

UI HOLDEN TOTAL PATIENT VOLUMES

22,842
FY 2015

23,937
FY 2016

25,391
FY 2017

26,683
FY 2018

28,296
FY 2019

18%

Growth in patient discharges in five years

FY 2019 PATIENTS IN IOWA

24,578

IOWA PATIENT VOLUMES BY COUNTY

5	1	10	6	31	14	16	16	15	21	17		
5	7	12	16	21	21	104	62	66	165	129		
11	20	21	13	41	50	34	128	215	1,167	227	142	789
36	7	20	48	188	52	86	89	193	231	2,301	216	269
6	8	35	36	76	247	206	164	216	370	5,023	370	757
4	5	5	30	97	1,117	164	216	370	5,023	370	1,010	3,089
15	7	16	35	108	149	139	254	669	228	1,010	1,010	1,010
4	7	5	27	20	27	48	391	327	409	629	629	629
3	21	8	13	14	28	79	65	157	649	649	649	649

HOLDEN COMPREHENSIVE CANCER CENTER COMMUNITY ADVISORY BOARD

The Holden Comprehensive Cancer Center Community Advisory Board consists of thought leaders, patient advocates, and other cancer stakeholders who live or work in Iowa. The board provides input and feedback to ensure that Holden's community outreach, engagement, and research activities are informed, promote health equity, and are responsive to the needs of Iowa's communities. The exchange of information and ideas between researchers, cancer center staff, and advisory board members ensures that values and cultural differences among persons and communities are respected. An active and representative community advisory board is vital to reducing the burden of cancer in Iowa's communities.



Community leaders from throughout Iowa gathered at the Holden Comprehensive Cancer Center Community Advisory Board's inaugural meeting on December 18, 2019, at the Iowa City Public Library. The group will collaborate with Holden on identifying the needs of their communities as they relate to reducing the burden of cancer.

University of Iowa Holden Comprehensive Cancer Center
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